

## **REMARKS**

### **Status of the Claims**

Claims 21-27 are pending.

No new matter has been added by way of the present submission. For instance, all pending claims have been cancelled and replaced with new claims 21-27. New claims 21-27 are supported by the claims and specification as originally presented and now further clarify the presently claimed invention. Thus, no new matter has been added.

In view of the following remarks, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

### **Priority Under 35 U.S.C. § 119**

Applicants thank the Examiner for acknowledging Applicants' claim for foreign priority under 35 U.S.C. § 119, and receipt of the certified priority document.

### **Information Disclosure Citation**

The Information Disclosure Statement (IDS) filed on May 10, 2006 allegedly fails to comply with 37 C.F.R. § 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

In this regard, Applicants are providing herewith a clean copy of the SB/08 listing the references originally cited in the May 10, 2006 IDS, as well as copies thereof. The Examiner is respectfully requested to consider these references on the record.

### **Issues Under 35 U.S.C. § 112, 1st Paragraph (Written Description and Enablement)**

Claims 1, 6-14 and 16 stand rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as failing to comply with the written description requirement.

Further, claims 1-16 stand rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph as failing to comply with the written description requirement.

Applicants respectfully traverse each of the above rejections and submit that the claims as now pending fully comply with the written description and enablement requirements of 35 U.S.C. § 112, 1<sup>st</sup> paragraph. In particular, the claims reflect the following changes:

- The definitions of substituents R<sup>1</sup> and R<sup>2</sup>, and R<sup>4</sup> and R<sup>5</sup> which are joined to form an optionally substituted 4-8 membered ring have been removed.
- The terms "derivatives" and "solvates" have been removed, and "isomers" are now "stereoisomers."
- The terms "heterocycle," "aryl" and "alkyl" are specifically defined by chain or ring size limitations.

Applicants respectfully submit that the claims, as amended, comply with the enablement and written description requirements of 35 U.S.C. § 112, 1<sup>st</sup> paragraph. Accordingly, reconsideration and withdrawal of these rejections are respectfully requested.

**Issues Under 35 U.S.C. § 102(a)/(b)/(e)**

Claims 1-9 and 16 stand rejected under 35 U.S.C. § 102(a) and § 102 (e) as being anticipated by Bridger, U.S. Patent 6,750,348 (hereinafter referred to as Bridger '348).

Further, claims 1-9, 12, 13 and 16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by A. R. Jacobson (hereinafter referred to as Jacobson).

These rejections are respectfully traversed. Complete discussions of the Examiner's rejections are set forth in the Office Action, and are not being repeated here.

The compounds of formula (1) in the presently pending claims are not anticipated by either Bridger '348 or Jacobson. Thus, the present invention is novel over these references. The Examiner is therefore respectfully requested to withdraw these rejections.

**Issue under 35 U.S.C. §103(a)**

Claims 1-16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Hu, U.S. Patent 6,495,715 (hereinafter referred to as Hu '715) in view of G. Patani (hereinafter referred to as Patani).

This rejection is respectfully traversed. A complete discussion of the Examiner's rejection is set forth in the Office Action, and is not being repeated here.

By way of the present amendment, the scope of compounds encompassed by formula (1) has been specifically defined. As discussed below, the cited art fails to suggest or disclose such subject matter, whether taken alone or in combination.

First, Hu '715 neither discloses nor suggests the compound of formula (1) in the amended claims. Furthermore, the compounds of Hu '715 relate to a calcium channel blocker which has a totally different action mechanism from a melanocortin receptor agonist of the present invention. Second, Patani merely discloses a myriad of possible modifications of known compounds, such as chloro substitution. However, neither Hu '715 nor Patani provides any suggestion or motivation by which a skilled artisan would have conceived the present invention. Therefore, the present invention is non-obvious over Hu '715 and Patani. Further discussion is provided below:

MPEP § 2143 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 148 USPQ 459, 467 (U.S. 1966), which provides the controlling framework for an obviousness analysis. The four *Graham* factors of: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims that are at issue; resolving the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). Secondly, the Examiner must provide some rationale for determining obviousness, wherein MPEP § 2143 set forth some rationales that were established in the recent decision of *KSR Int'l Co. v Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007).

It was also recognized in *Dennison Mfg. Co. v. Panduit Corp.*, 475 U.S. 809, 229 USPQ 478 (1986) that one should not rely on hindsight, and that "in addressing the question of obviousness a judge must not pick and choose isolated elements from the prior art and combine them so as to yield the invention in question if such a combination would not have been obvious at the time of the invention." 475 U.S. at 810. Indeed, in *Graham v. John Deere Co.*, *supra*, the Supreme Court recognized that the obviousness inquiry must "guard against slipping into use of hindsight and to resist the temptation to read into the prior art the teachings of the invention in issue." *Id.* at 36. The result of these holdings is that an Examiner may not simply pick and choose only those selective portions of the reference, which support the Examiner's position.

Further, the Examiner must provide some rationale for asserting obviousness. M.P.E.P. § 2143 sets forth some rationales that were established in the recent decision of *KSR Int'l Co. v Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). The teaching, suggestion, motivation test is a valid test for obviousness, but one which cannot be too rigidly applied. *See KSR Int'l*, *supra*.

While the courts have adopted a more flexible teaching/suggestion/motivation (TSM) test in connection with the obviousness standard based on the *KSR* case which involved a mechanical device in a relatively predictable technological area, it remains true that, despite this altered standard, the courts recognize inventors face additional barriers in relatively unpredictable technological areas. The determination of obviousness is dependent on the facts of each case in view of the totality of the circumstances. *See Graham*, 383 U.S. at 17-18; *see, e.g., In re Dillon*, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (*en banc*); M.P.E.P. § 2144.08(II).

In the present instance, the Examiner has asserted that the presently pending claims are obvious over Hu '715 in view of Patani. According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the genus of compounds of Hu '715 to create para-chloro substituted benzenes (such falling within the scope of "substituted benzenes" of Hu). The Examiner rationalizes that Patani teaches that a chloro substitution is a common method of modifying known compounds to alter metabolic profiles, and thus, one of ordinary skill in the art would readily make such a replacement. Applicants respectfully disagree with the Examiner.

Applicants submit that the presently claimed compounds could not be easily arrived at by one of ordinary skill in the art. In fact, the number of possible permutations of Hu '715 even when not combined with Patani is so enormous that, given no direction, any one of the compounds therein could serve as a starting point (e.g., a "lead" compound) for experimentation. However, one of skill in the art would have to make numerous selections and modifications from within the disclosure of Hu '715, and then decide to make a para-chloro benzene substitution. All this time, the skilled artisan would have to first ignore all of the other possible preferences of Hu '715 and then only select one of the myriad of possible "allegedly analogous" substitutions discussed in Patani. Certainly this cannot amount to a legally sufficient rejection.

To this end, it is noted that Hu '715 fails to provide any concrete examples that are even close to the presently claimed invention. Rather, one must make numerous selections and indeed modifications based upon the enormous disclosure of Hu '715 even though given no direction to do so. Of particular relevance is the Federal Circuit decision *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007), which makes clear that one skilled in the art would select the "best" compound as a "lead compound" after looking at all of the

available prior art. 83 USPQ2d at 1176 (“the prior art did not suggest to one of ordinary skill in the art that compound b would be the best candidate as the lead compound for antidiabetic research”). In the *Takeda* case, an argument was submitted that a certain compound (compound b) would be selected as a “lead compound.” However, the court found that there was “nothing in the prior art to narrow the possibilities of a lead compound to compound b.” 83 USPQ2d at 1176-1177. The same is true in the present instance. There is nothing to indicate that any particular compound of Hu ‘715 should be selected. There is simply an enormous number of potential compounds, any number of which could be a starting point.

Next, according to the Examiner, one of skill in the art would make a para-chloro benzene substitution based upon the teachings of Patani. However, this is an overly simplified explanation since the teachings of Patani, although indicating that chloro substitutions are possible, in fact, encompass a vast number of so-called “bioisosteres.” Such possible changes discussed in Patani include (1) fluorine vs. hydrogen replacements, (2) interchange of hydroxyl and amino groups, (3) interchange of hydroxyl and thiol groups, (4) divalent replacements involving double bonds, (5) divalent replacements involving two single bonds, (6) trivalent atoms and groups, (7) tetrasubstituted atoms, (8) ring equivalents, (9) divalent ring equivalents, (10) trivalent ring equivalents, (11) cyclic vs. noncyclic nonclassical bioisosteric replacements, etc., just to name a few.

It is not seen why one of skill in the art would take this enormous disclosure as specifically directing the generation of any particular modification, let alone a para-chloro benzene substitution. Indeed, would such a skilled artisan not select any number of these possible substitutions?

Applicants submit that the above number of selections are simply too improbable. There is simply no reason to prepare the compounds of the present invention. Applicants further direct the Examiner’s attention to the well-established teachings of *Ex parte Kuhn* and *In re Baird*. The fact that a claimed product is within the broad field of the prior art and one might arrive at it by selecting specific items and conditions does not render the product obvious in the absence of some directions or reasons for making such selection. *Ex parte Kuhn*, 132 USPQ 359 (POBA 1961). Similarly, a compound within the scope of a generic formula which encompasses more than 100 million compounds cannot render a product obvious absent some direction or reasons

for selecting the substituents required to arrive at the compound. *In re Baird*, 29 USPQ2d 1550, 16 F.2d 380 (Fed. Cir. 1994).

At best the Examiner's rationale amounts to one of the two identified erroneous classes of "obvious to try" rejection. The issue of "obvious to try" was recently revisited by the Federal Circuit in *In re Kubin* (2008-1184, decided April 3, 2009). The court highlighted an earlier decision of *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988), where it was cautioned that "obvious to try" is an incantation whose meaning is often misunderstood:

It is true that this court and its predecessors have repeatedly emphasized that "obvious to try" is not the standard under § 103. However, the meaning of this maxim is sometimes lost. Any invention that would in fact have been obvious under § 103 would also have been, in a sense, obvious to try. The question is: when is an invention that was obvious to try nevertheless nonobvious?

*In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

The Federal Circuit held in *In re Kubin* that to differentiate between proper and improper applications of "obvious to try," it is necessary to understand two classes of situations where "obvious to try" is erroneously equated with obviousness under § 103. In the first class of cases,

what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

*Id.* In such circumstances, where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness. The inverse of this proposition is succinctly encapsulated by the Supreme Court's statement in *KSR* that where a skilled artisan merely pursues "known options" from a "finite number of identified, predictable solutions," obviousness under § 103 arises. 550 U.S. at 421.

The second class of *O'Farrell's* impermissible "obvious to try" situations occurs where what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

853 F.2d at 903. Again, *KSR* affirmed the logical inverse of this statement by stating that § 103 bars patentability unless "the improvement is more than the predictable use of prior art elements according to their established functions." 550 U.S. at 417.

In the present instance, Applicants submit that the Examiner has participated in the first of the above two classes of impermissible "obvious to try" analysis. Nowhere in the prior art is the particular requirement for the claimed combination of rings and substituents ever discussed. While such a combination might hypothetically fall within the generic disclosure of Hu '715c combined with Patani, the Examiner's rationale certainly amounts the throwing of metaphorical darts at a board filled with combinatorial prior art possibilities. This is clearly the first of the two common "obvious to try" pitfalls decidedly admonished by the Federal Circuit.

### Conclusion


All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie, Registration No. 42,874 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By   
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**Attachments:** SB/08 and copies of references from May 10, 2006 IDS